REMARKS

Applicants respectfully request reconsideration. Claims 1-20 and 27-30 were previously pending in this application. By this amendment, Applicants are amending claim 1 to clarify that the sample is filtered through the filter. Support for the amendment can be found in the specification as filed at least at page 5, lines 21-22; page 14 in the descriptions for Figures 9, 10, and 11; and page 19, line 19. Claim 1 has also been amended to include the term amyloid-like with each reference to "fibrils" to make the language in the claim consistent. Support for the amendment can be found in claim 1 as filed. Claims 17, and 28-30 have also been amended to correct an erroneous antecedent basis. New claims 31 and 32 have been added. Support for the new claims can be found in the specification as filed at least at page 7, lines 9-10, page 20, lines 7-9, and Example 5 at page 23. As a result, claims 1-20 and 27-32 are pending for examination with claim 1 being an independent claim. No new matter has been added.

Allowable Subject Matter

Applicants acknowledge that the Examiner indicates at paragraph 8 on page 5 of the Office Action that claims 13-16 are clear of the prior art of record and that the claims would be allowable if rewritten in independent form including all of the limitations of the base claims and any intervening claims.

Rejections Under 35 U.S.C. §102

The Examiner rejected claims 1-6, 8-12, and 27-30 under 35 U.S.C. §102(a) as being anticipated by Kalchman et al. (WO 97/18825). Applicants respectfully traverse the rejection.

To support a case for anticipation, the cited reference must teach each element of the claimed invention. Applicants submit that the Kalchman et al. reference does not teach each element of the amended claim 1 and therefore does not anticipate the invention.

Applicants have amended claim 1 to clarify a distinction between the instant claimed invention and the blotting method described in the Kalchman et al. reference. The method set forth in amended claim 1 for detecting the presence of detergent-or urea-insoluble amyloid-like fibrils or protein aggregates in a sample on a filter includes contacting the filter with material of a sample suspected to include fibrils or aggregates which has been previously treated with detergent or urea to solubilize the sample and *filtering the sample through the filter* to capture the

detergent- or urea-insoluble amyloid-like fibrils or protein aggregates; and detecting whether the fibrils or aggregates are retained on the filter.

In contrast, the Kalchman et al. reference teaches *blotting* samples from a gel onto a PVDF membrane and does not teach or suggest filtering a sample through a membrane and therefore does not anticipate the claimed invention. One of ordinary skill in the art would recognize that in the Kalchman et al. reference the proteins from a gel are blotted onto a PVDF membrane – and are not filtered through a filter.

Additionally, Applicants submit that as described in the Kalchman et al. reference, the proteins that are blotted onto a PVDF membrane are contained in the supernatant obtained from a centrifugation step and have been electophoretically separated on SDS-PAGE. The SDS-PAGE technique includes solubilizing proteins in SDS, a detergent. Applicants submit that the proteins blotted in Kalchman et al are proteins that are soluble in detergent. In contrast, the method set forth in amended claim 1 includes the detection of detergent- or urea-*insoluble* fibrils or proteins aggregates that are collected on a filter upon filtering the sample through a filter. The fibrils and/or protein aggregates separated in the instantly claimed methods are not soluble in detergent and the Kalchman et al. reference does not teach or suggestion the detection or collection of detergent- or urea-insoluble proteins.

Because the instantly claimed invention includes the step of filtering a sample through a filter and the claims are drawn to the detection of detergent- or urea-insoluble fibrils or protein aggregates and the Kalchman et al. reference fails to teach or suggest these elements of the claimed invention, Applicants submit that the reference does not anticipate the invention as claimed. Therefore, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1-6, 8-12, and 27-30 under 35 U.S.C. §102(a) as being anticipated by Kalchman et al. (WO 97/18825).

Rejections Under 35 U.S.C. §103

The Examiner rejected claim 6 under 35 U.S.C. §103(a) as being unpatentable over Kalchman et al. (WO 97/18825) in view of Yanai et al. (US Patent 6,743,422). Applicants respectfully traverse the rejection.

As described above herein, the instantly claimed invention includes methods for detecting the presence of detergent- or urea-insoluble amyloid-like fibrils or protein aggregates in a sample

on a filter. The claimed methods include contacting the filter with material of a sample suspected to include fibrils or aggregates that has been previously treated with detergent or urea to solubilize the sample and filtering the sample through the filter to capture the detergent- or urea insoluble amyloid-like fibrils or protein aggregates, with the soluble components passing through the filter; and detecting whether the fibrils or aggregates are retained on the filter.

To support a *prima facie* case for obviousness, the Examiner must show all elements of the claimed invention are present in the references, specific motivation to combine the teaching of the references to make the claimed invention, and a likelihood that the combination would result in the instantly claimed invention. These requirements are not met in this case.

Applicants submit that the Kalchman et al. reference describes blotting proteins from a gel onto a PVDF membrane. The Yanai et al. reference discloses hydrophilic membranes having low adsorptivity for protein. Neither reference describes or suggests filtering a sample through a filter to detect detergent- or urea-insoluble fibrils or protein aggregates. Thus, the references do not teach all elements of the claimed invention.

In addition, Applicants submit that even if all elements of the claimed invention were present in the references cited by the Examiner, the Kalchman et al. reference in fact teaches away from using a low protein adsorption filter, which is the type of filter described in the Yanai et al. reference. As described above herein, the Kalchman et al. reference teaches separating/collecting proteins by blotting a sample of proteins onto a membrane. As is recognized in the art, proteins are blotted from a gel onto a membrane in order to retain the proteins from the gel on the membrane. The Kalchman et al. reference specifically teaches blotting onto a PVDF membrane. PVDF membrane is notably a membrane with high protein retention properties, properties that one of ordinary skill in the art would understand to be desirable in a membrane used for blotting because of its properties of high protein adsorptivity.

In contrast to the Examiner's characterization of PVDF membrane at page 3, paragraph 5 of the Office Action, as a "low protein adsorptivity filter", Applicants submit that the PVDF membrane Immobilon-P, which is the membrane disclosed in the Kalchman et al. reference, is described by its manufacturer as desirable for use because of its high protein adsorptivity, a feature directly in contrast with the filter characteristics set forth in claim 6, namely a low capacity for protein adsorption. (See Manufacturer's publication provided herewith).

Applicants submit that based on the Kalchman et al. reference, one of ordinary skill in the art would not be motivated to use a filter with a *lower* protein retention, such as that taught in Yanai et al. reference – as the goal of blotting from a gel is to retain the soluble proteins. Therefore, Applicants assert that the Kalchman et al. reference would discourage one of ordinary skill in the art from using a filter as taught in the Yanai et al. reference, and that one of ordinary skill in the art would not be motivated to combine methods described in Kalchman et al. with those of Yanai et al. to use a filter with a *lower* protein retention than that of the PVDF membrane taught in the Kalchman et al. reference.

Applicants submit that all of the elements in the claimed methods are not present in the cited references and no specific motivation to combine the teaching of the references to make the claimed invention has been provided. Thus, a *prima facie* case for obviousness has not been made.

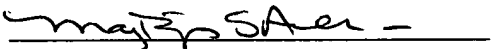
Accordingly, Applicants request reconsideration and withdrawal of the rejection of claim 6 under 35 U.S.C. §103(a) as being unpatentable over Kalchman et al. (WO 97/18825) in view of Yanai et al. (US Patent 6,743,422).

CONCLUSION

A Notice of Allowance is respectfully requested. The Examiner is requested to call the undersigned at the telephone number listed below if this communication does not place the case in condition for allowance.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicants hereby request any necessary extension of time. If there is a fee occasioned by this response, including an extension fee that is not covered by an enclosed check, please charge any deficiency to Deposit Account No. 23/2825.

Respectfully submitted,
Erich Wanker et al., Applicants

By: 

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Docket No.: V0179.70001US00
Date: May 23, 2005
x05/23/05x

Immobilon™ Transfer Membranes

For superior protein and nucleic acid blots

Membranes for:

- *Westerns*
- *Dots/slots*
- *Southerns*
- *Northerns*
- *Colony/plaque lifts*

Protein Applications

Immobilon-P Membrane

The original, and most commonly used, PVDF transfer membrane for western blotting. It has a 0.45 µm pore size and is recommended for blotting proteins >20 kDa.

- Compatible with a variety of detection chemistries, including radioactive, chromogenic, and chemiluminescent techniques
- High protein adsorption and retention ensures greater sensitivity
- Won't crack or curl like nitrocellulose. Can be cut without fracturing and reprobed multiple times
- Our Rapid Immunodetection Protocol eliminates the need for blocking and reduces detection times by up to 2 hours

Immoilon-P^{SQ} Membrane

This PVDF membrane has a 0.2 µm pore size. The large internal structure results in higher protein adsorption and sequencing yields than other membranes. Recommended for blotting proteins <20 kDa and sequencing.

- Higher capacity and retention than 0.45 µm membranes
- Prevents blow-through of low molecular weight proteins
- Compatible with a variety of detection chemistries, including radioactive, chromogenic, and chemiluminescent techniques

New!

Immobilon-FL Membrane

The first transfer membrane optimized for fluorescence applications. This PVDF membrane exhibits extremely low background fluorescence.

- Compatible with all commonly used fluorescent dyes
- Can be used at all excitation and emission wavelengths. Ideal for multiplexing
- Quality tested to ensure low background fluorescence in western blotting applications
- Also compatatible with non-fluorescent detection chemistries

Nucleic Acid Applications

Immobilon-Ny+ Membrane

A positively charged nylon membrane optimized for reliable and reproducible transfer, immobilization, hybridization, and subsequent reprobing.

- Provides maximum sensitivity with minimal background due to the density and uniformity of the positively charged surface
- Has exceptional retention and reprobing characteristics. Studies show 50% greater signal than other positively charged nylon membranes — 5x greater after 12 reprobes
- Performs well in both chemiluminescent and radioactive detection systems
- Can be used to detect sub-picrogram amounts of DNA and RNA

Immobilon-NC Membranes

An economical alternative for nucleic acid and protein blotting protocols.

- Immobilon-NC (HAHY) membrane is a mixed cellulose esters matrix with surfactants that improve wettability and handling during the transfer process.
- Immobilon-NC (HATF) membrane is a mixed cellulose esters matrix with no surfactants that can interfere with cell wall integrity during cell growth. Recommended for colony lifts.

New!

Blotting Sandwiches with Immobilon-P Membrane

- Immobilon-P membrane interleaved with two sheets of pre-cut blotting paper offers convenience and time savings for high throughput labs. Available in sizes to match most pre-cut gels. See Ordering Information for cut sizes.

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